26. (New) The method of claim 22 wherein activation of the signal transduction pathway results in release of insulin from pancreatic ß-cells.

27. (New) The method of claim 22 wherein activation of the signal transduction pathway results in release of catecholamines from chromaffin cells.—

REMARKS

Claims 6-8 are pending in the application. The pending claims are rejected under 35 U.S.C. § 112 first and second paragraph and under 35 U.S.C. § 103(a). Applicants have amended claims 4-6 to more particularly point out and distinctly claim the invention. New claims 17-27 have been added. No new matter has been added by amended claims 4-6 or by the addition of new claims 17-27. For reasons detailed below, the rejections should be withdrawn and the claims allowed to issue. Entry of the foregoing amendments is respectfully requested.

1. The Claims are Enabled

Claims 4-6 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that the distinct steps for the regulation of biological activity critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure.

The test for enablement is whether one reasonably skilled in the art could make and use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F. 2d. 778, 8 USPQ 2d 1217. Furthermore, a patent need not teach, and preferably omits, what is well known in the art. *Hybridtech Inc., v. Monoclonal Antibodies, Inc.* 802 F 2d., 1367, 231 USPQ 81 (Fed. Cir. 1986).

Applicants contend that the present invention is based on the discovery that IAA-RP and IAA-R bind to an imidazoline receptor resulting in activation of the receptor mediated signal transduction pathway. For example, Example 6 of the specification describes contacting membrane preparations expressing an imidazoline receptor with IAA-RP or IAA-RP and that such exposure results in release of arachidonic acid, a known imidazoline receptor mediated response. In addition, Example 7 of the specification describes experiments demonstrating that exposure of pancreatic cells expressing an imidazoline receptor, to IAA-RP or IAA-RP results in insulin release. Based on this disclosure, coupled with methods disclosed in the specification for administering compositions comprising IAA-RP or IAA-RP (p.24, line 5 through p.25, line 8), the pending claims are fully enabled for the entire scope of the recited subject matter. Therefore, the rejections under 35 U.S.C. §112, first paragraph, should be withdrawn.

2. The Claims are Definite

Claim 6 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Examiner, the claim is indefinite because the term congener is not defined by a structural formula or chemical name.

Applicants maintain that Claim 6 is definite because the term congener is a term of art and one of skill in the art would understand the meaning of the term congener. For example, Dorland's Illustrated Medical Dictionary (25th edition, 1974, John P. Friel (Dictionary Editor for the Publisher); W. B. Saunders, Philadelphia) defines a congener as "a chemical compound closely related to another and exerting similar or antagonistic effects." In addition, the specification clearly defines the meaning of the term "congener." In this regard, the Examiner's attention is respectfully directed to p. 8, line 17 through p.9, line 16 of the specification which clearly defines the term "congener."

In view of the foregoing comments, the rejections under 35 U.S.C. §112, second paragraph, should be withdrawn.

3. The Claimed Invention is Not Obvious

Claims 4-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over United States Patent No. 5,681,947 ("the '947 patent"). The Examiner alleges that it would have been obvious to one having ordinary skill in the art at the time the invention was made to administer the instantly claimed active agents to affect biological activity

because the prior art clearly indicates that the skilled artisan would be quite capable of affecting biological activity using the disclosed compounds of the prior art.

Applicants respectfully disagree with the Examiner's rejection and submit that the claimed invention is not rendered obvious by the cited reference using the objective standard for obviousness under 35 U.S.C. §103. As set forth in *Graham v. Deere*, a finding of obviousness under 35 U.S.C. §103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v Deere, Inc.* 383 U.S. 1 (1966).

Applicants contend that the present invention is based on the discovery that IAA-RP and IAA-R bind to an imidazoline receptor resulting in activation of the receptor mediated signal transduction pathway. Thus, in the present instance, the proper inquiry is whether the cited '947 patent teaches or suggests the claimed methods for regulating an imidazoline receptor signal transduction pathway. Clearly the answer to this question is no. In fact, a survey of the '947 patent indicates that the patent fails to mention the modulation of any receptor, much less an imidazoline receptor.

Applicants assert that in the present instance, the Examiner has failed to produce any reference that teaches or suggests the modulation of an imidazoline receptor. Therefore, the claimed invention is not obvious, and the rejections under 35 U.S.C. §103 should be withdrawn.

CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by the amended claims is patentable over the rejections of the Examiner. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

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Lisa B. Kole
Patent Office Reg. No. 35,225

Carmella L. Stephens
Patent Office Reg. No. 41,328

BAKER BOTTS L.L.P.
30 Rockefeller Plaza
New York, New York 10112-0228

Attorneys for Applicants
(212) 408-2500

APPENDIX A

IN THE CLAIMS:

Please amend the claims as follows:

4. (amended) A method of regulating the [biological activity of an imidazoline receptor comprising contacting said receptor with] signal transduction pathway mediated by binding of an imidazoleacetic acid-ribotide to an imidazoline receptor comprising the step of contacting said receptor expressed in a cell with the imidazoleacetic acid-ribotide.

5. (amended) A method of regulating the [biological activity of an imidazoline receptor comprising contacting said receptor with] signal transduction pathway mediated by binding of an imidazoleacetic acid-ribotide to an imidazoline receptor comprising the step of contacting said receptor expressed in a cell with the imidazoleacetic acid-riboside.

6. (amended) A method of regulating the [biological activity of an imidazoline receptor comprising contacting said receptor with imidazoleacetic acid-ribotide or imidazoleacetic acid-riboside congener] signal transduction pathway mediated by binding of an imidazoleacetic acid-ribotide congener or imidazoleacetic acid-riboside congener to an imidazoline receptor comprising the step of contacting said imidazoline receptor with said congener.

Please add the following claims:

--17. (New) The method of claim 4 wherein the methylene group is substituted for the oxygen atom that links the 5' carbon to the phosphate atom in the imidazoleacetic acid-ribotide.

18. (New) The method of claim 4 wherein the imidazoleacetic acid-ribotide is a 2' or 3' deoxy-IAA-RP.

19. (New) The method of claim 4 wherein the imidazoleacetic acid-ribotide is a carboxy-methyl or carboxy-ethyl ester of IAA-RP.

20. (New) The method of claim 4, 5, or 6 wherein furan is linked to the number 2 carbon atom of the imadazole ring.

21. (New) The method of claim 4, 5, or 6 wherein furan is linked to the nitrogen closest to the methylene-carboxy side chain of the imidazole ring.

22. (New) The method of claim 4, 5 or 6, wherein the imadazole ring is converted to an imadzoline ring.

23. (New) The method of claim 4, 5 or 6 wherein the signal transduction pathway is activated.

24. (New) The method of claim 4, 5 or 6 wherein the signal transduction pathway is repressed.

25. (New) The method of claim 22 wherein activation of the signal transduction pathway results in release of arachidonic acid.

26. (New) The method of claim 22 wherein activation of the signal transduction pathway results in release of insulin from pancreatic ß-cells.

27. (New) The method of claim 22 wherein activation of the signal transduction pathway results in release of catecholamines from chromaffin cells.--